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Oral presentations

1 – NIKITA KOSTER

MULTI-OMICS ANALYSIS IDENTIFIES COMMON MOLECULAR SIGNATURES IN PSORIASIS TARGET LESIONS OF VARYING SEVERITIES DURING GUSELKUMAB TREATMENT

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Background Multi-omics profiling, including bulk transcriptomics, interstitial fluid (ISF) lipidomics, skin surface lipidomics, and spatial lipidomics, enables in-depth characterization of psoriasis pathobiology. Inter-individual differences in these profiles may influence treatment response.
Objective To determine whether phenotypically similar plaques in mild and moderate-to-severe psoriasis differ molecularly, and to assess the effects of IL-23 blockade with guselkumab on transcriptomic and lipidomic profiles across disease severities.
Methods Twenty patients with mild psoriasis (PASI ≤ 5) and six with moderate-to-severe disease (PASI ≥ 10) were enrolled, each with at least one target plaque on the extremities. Skin punch biopsies, tape strips, and peri-lesional suction blisters were collected before, during, and after 16 weeks of guselkumab therapy, alongside samples from ten healthy controls. Multi-omics analyses included RNA sequencing, LC-MS metabolomics, and mass spectrometry imaging.
Results At baseline, plaques were comparable across groups in erythema, scaling, and induration. Transcriptomic profiling revealed similar molecular signatures in both severity groups versus healthy controls, with elevated Th17- and modestly increased Th2-related gene expression. Only twelve genes differed significantly, all with small fold changes ($log_2FC < 1$). Perilesional ISF metabolomics showed normalization of inflammatory lipid mediators (15-HETrE, S1P 18:2, S1P 16:1, 11-HETE) during treatment. Clinical, imaging, and molecular data indicated comparable therapeutic responses.
Conclusion Phenotypically similar plaques in mild and moderate-to-severe psoriasis share comparable molecular profiles, supporting IL-23 blockade with guselkumab as a relevant treatment for mild disease.

2 – EMMA HOLTAPPELS

HIJACK VITILIGO: JAK3 AND TEC FAMILY KINASE INHIBITION IN THE PATHOGENESIS AND TREATMENT OF VITILIGO

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Background Vitiligo is an autoimmune disease, characterized by depigmented skin-lesions due to melanocyte destruction. Current therapies have limited efficacy and often result in relapse, likely due to persisting tissue-resident memory T-cells (TRM), depending on IL-15 signaling via JAK3. Ritlecitinib is a novel, irreversible JAK3/TEC-family kinase-inhibitor through which TRM may be targeted in vitiligo.
Objective To elucidate the expression profile of JAK3/TEC-family kinases in vitiligo and assess whether ritlecitinib offers a durable treatment option.
Methods The JAK3/TEC family kinase (ITK/BTK/TEC) expression profile was analyzed on the RNA-level using publicly-available scRNAseq-datasets and on the protein-level using multiplex-immunohistochemistry, focusing on skin cells and T-cell subsets in healthy and vitiligo skin (n=13). Cellular effects of ritlecitinib were investigated in melanocyte/T-cell co-cultures and human vitiligo skin-explants.
Results In vitiligo skin, levels of JAK3/TEC-family kinase-expressing cells were increased compared to healthy skin. JAK3/TEC-family kinases were predominantly expressed by T-cells,

but, unexpectedly, keratinocytes also expressed JAK3/TEC-family kinases more frequently in vitiligo skin. Specific JAK3/TEC-family kinase inhibition using ritlecitinib effectively reduced *in vitro* cytotoxic activity of T-cells against melanocytes, showing a durable effect upon re-exposure to melanocytes without additional ritlecitinib treatment. Decreased melanocyte apoptosis was also seen in skin-explants. Ritlecitinib also reduced chemokine release from stimulated keratinocytes.
Conclusion We characterized expression of JAK3/TEC-family kinases and found significant, cell-type-dependent differential expression in vitiligo versus healthy skin. Ritlecitinib not only effectively inhibited T-cell activation, thereby reducing melanocyte apoptosis, but also reduced chemokine release from keratinocytes. Therefore, ritlecitinib has the potential to meet the requirements for effective repigmentation therapy in vitiligo.

3 – HIDDE SMITS

INHIBITION OF THE IL-4/L-13 SIGNALING PATHWAY INDUCES TYPE I IMMUNE ACTIVATION IN CONJUNCTIVA EPITHELIAL CELLS

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Background Both dupilumab and tralokinumab are monoclonal are highly effective in treating moderate-to-severe atopic dermatitis. Dupilumab blocks the shared IL-4Rα subunit, thereby inhibiting both IL-4 and IL-13 signaling, in contrast tralokinumab selectively binds the IL-13 molecule. The most common side effect of these treatments is ocular surface disease (OSD). The mechanisms underlying these adverse effects remain poorly understood.
Objective This study aimed to investigate the transcriptional mechanisms underlying OSD in non-immune conjunctival cells following dupilumab and tralokinumab treatment.
Methods Eyeprim samples were collected from 6 dupilumab-treated patients, 6 tralokinumab-treated patients (at baseline and after four weeks), and six non-atopic controls. Conjunctival epithelial cells were analyzed by single-cell RNA sequencing.
Results Computational analysis revealed three main epithelial populations: basal cells, superficial epithelial cells, and immune-activated superficial epithelial cells. Compared with non-atopic controls, showed no significantly enriched pathways in either population, although weak immune activation was evident through upregulation of HLA-DQA1 and IL6R in epithelial cells. Following dupilumab treatment, immune-activated superficial epithelial cells expanded and displayed an IFNγ-driven type 1 immune signature, characterized by increased CXCL1, CXCL6, CXCL9, CXCL10, CCL20 and HLA-DR expression, suggesting increased activation and immune cell recruitment. Tralokinumab treatment induced a similar but less pronounced response.
Conclusion IL-4/IL-13 pathway inhibition induces a conjunctival T1 immune response, which is more pronounced with dual IL-4/IL-13 blockade than with selective IL-13 inhibition by tralokinumab. These findings align with the clinical manifestations of ocular surface disease observed in treated patients and provide translational insights that may inform therapeutic decision-making.

4 – ANNE-LISE STRANDMOE

ALTERED PRO-INFLAMMATORY B CELL CYTOKINE RESPONSES IN PEMPHIGUS VULGARIS: IMPACT OF PRIOR RITUXIMAB TREATMENT

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Background Pemphigus vulgaris (PV) is a B cell–mediated autoimmune blistering disease characterized by loss of epidermal and/or mucosal adhesion due to autoantibodies predominantly targeting desmoglein 3. Although B cell–depleting therapy with rituximab has revolutionized PV treatment, disease relapse remains common, and the immunological mechanisms underlying relapse are not fully understood.
Objective To assess whether differences in pro- and anti-inflammatory cytokine production by B cells distinguish patients with active PV from healthy controls, and to explore whether prior rituximab treatment or relapse-prone patients are associated with altered B cell functional profiles.
Methods PBMC samples were collected from 29 active PV patients and age/sex-matched healthy controls (HC). Among PV patients, 11 were rituximab-naive (nPV) and 18 were rituximab-non-naive (nnPV), having previously received rituximab and subsequently relapsed. At sampling, 72% of nPV and 22% of nnPV were receiving prednisone. PBMCs were cultured using CpG for 3 days, and BFA, PMA, and CaI for 5 hours for maximal stimulation. Intracellular cytokine (IL-10, TNFα, IL-6) production was analyzed by flow cytometry.
Results Patients with PV showed a reduced frequency of $TNF\alpha^+$ B cells compared with HCs (8,8% vs. 18,6% of B cells). Within the PV cohort, nnPV patients displayed a significant decrease in $TNF\alpha^+$ (6,3% vs. 20,7% of B cells) and $IL\text{-}6^+TNF\alpha^+$ B cells (0,71% vs. 2,35% of B cells) compared with nPV patients.
Conclusion These findings suggest a lasting alteration in the pro-inflammatory capacity of B cells, which may reflect either long-term effect of prior rituximab treatment or features associated with relapsing patients.

5 – MARGOT STARRENBURG

IMPACT OF TRALOKINUMAB ON CIRCULATING AND SKIN IMMUNE CELL LANDSCAPE IN PATIENTS WITH ATOPIC DERMATITIS

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Background Tralokinumab, an IL-13 targeting mAb, is an effective treatment for atopic dermatitis (AD). Th2 signaling disruption by IL-4Ra blockade had a strong functional immunological effect in AD patients, particularly on skin-homing T-cells. Skin resident T-cells have been associated with recurrent inflammatory skin diseases, such as AD.
Objective To study changes in (skin-homing) T-cell dynamics systemically and local (skin resident) T-cell function and distribution induced by selective IL-13 signaling blockade in AD.
Methods Blood samples of 22 AD patients and skin samples of 10 AD patients were collected longitudinally during tralokinumab treatment. PBMCs were characterized in flowcytometric assays, skin biopsies were studied using Imaging Mass Cytometry (IMC).
Results Mean EASI scores and serum TARC levels decreased significantly during treatment. Flow cytometry revealed a decrease in type 2 cytokine production and proliferation of skin-homing T-cells during treatment. IMC analysis enabled characterization of immune cell clusters in both the dermis and epidermis, including various myeloid cell types and several subsets of T-lymphocytes, amongst which OX40+, cytokine producing CD103+CD69+ skin resident CD4+ T-cells (CD4+ Tsr). The proportion of CD4+ Tsr decreased in the epidermis, but remained present in the dermis. Additionally, TARC producing myeloid cells and interferon gamma producing T-cells were significantly reduced in AD-lesional skin after tralokinumab treatment, while regulatory T-cell presence was increased.
Conclusion Systemically, tralokinumab reduces type 2 inflammation and serum TARC levels. Locally, attenuated AD activity by a reduction in TARC production and decreased cytokine producing CD4+ Tsr in the epidermis was observed, while dermal CD4+ Tsr persist.

6 – FLORENTINE DE BOER

SKIN BARRIER BIOMARKERS IN PATCH-INDUCED AND CLINICAL ALLERGIC AND IRRITANT CONTACT DERMATITIS

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Background Skin barrier impairment is central to irritant (ICD) and allergic contact dermatitis (ACD). *Stratum corneum* (SC) components cholesterol sulphate (CholSulph), glucosylcholesterol (CholGlc), and natural moisturizing factor (NMF) are critical for barrier function, but their changes in ICD and ACD remain underexplored.
Objective To measure CholSulph, CholGlc, NMF, and IL-1α, in patch-induced ICD and ACD, and in hand dermatitis (HD) diagnosed as ICD or ACD.
Methods SC samples were collected from HD patients undergoing patch testing. Biomarkers were analyzed in positive reactions to sodium lauryl sulfate (ICD, n = 44), allergens (ACD, n=113; nickel, chromium, methylisothiazolinone (MI)), lesional HD skin (n = 45) and control (empty chamber, n=121).
Results CholGlc was significantly elevated in patch-induced ICD and ACD. CholSulph increased in ICD and chromium- and MI induced ACD. NMF decreased in ICD, while IL-1α decreased in ICD and chromium ACD. Chromium induced the strongest response, nickel the weakest. In HD, ICD and ACD showed elevated CholGlc, reduced NMF and IL-1α, with CholSulph increased only in ACD. No biomarker differences were detected between clinical ICD and ACD.
Conclusion Both induced and clinical ICD and ACD show consistent SC biomarker changes reflecting barrier dysfunction, with no differences between clinical ICD and ACD.

7 – LIAN VAN DER GANG

SKIN BARRIER CHANGES IN ATOPIC DERMATITIS TREATED WITH BIOLOGICS AND JAK INHIBITORS

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Background Atopic dermatitis (AD) is strongly associated with impaired skin barrier function and altered *stratum corneum* lipid composition, particularly changes in ceramide levels. Skin barrier assessment can be clinically useful for lesion follow-up and therapy evaluation.
Objective To characterize skin barrier changes during biologic or Janus kinase inhibitor (JAKi) treatment using electrical impedance spectroscopy (EIS) and ceramide profiling.
Methods *Stratum corneum* impedance and deeper layer impedance were measured on lesional and non-lesional volar forearm skin of adult AD patients starting biologics (n=39) or JAKi (n=10) at baseline, week 4, and week 16. Controls included psoriasis patients (n=10) and healthy controls (n=10). Ceramides are currently being analyzed using liquid chromatography-mass spectrometry.
Results At baseline, both lesional and non-lesional EIS scores were significantly lower in AD patients compared to healthy controls and psoriasis patients. By week 16, both *stratum corneum* impedance and deeper layer impedance improved significantly, and *stratum corneum* impedance no longer significantly differed from healthy controls. When comparing treatment groups, no significant differences in EIS change after 16 weeks of treatment were found. However, JAKi induced greater EIS change at week 4 than biologics. Preliminary ceramide analysis shows partial normalization of the ceramide subclass composition and chain length with treatment.
Conclusion Systemic treatment with biologics and JAKi recovers skin barrier function in AD, as objectively measured by EIS. Barrier recovery was faster with JAKi, although differences levelled out by week 16. During treatment, EIS approached those of healthy controls, supporting its utility to monitor treatment response.

8 – CATHERINE MERGEN

STRATUM CORNEUM CERAMIDE ALTERATIONS AND BARRIER DYSFUNCTION IN CUTANEOUS T-CELL LYMPHOMA AND THEIR RESPONSE TO CHLORMETHINE TREATMENT

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Background Mycosis fungoides (MF) is the most common subtype of primary cutaneous T-cell lymphoma, in which malignant T lymphocytes infiltrate the skin, resulting in patches, plaques, and eventually tumors, which are associated with a reduced skin barrier function. The *stratum corneum* lipid matrix is essential for maintaining an intact skin barrier and alterations in lipid composition, especially ceramides, have been associated with a reduced barrier function in inflammatory skin conditions.
Objective To characterize the *stratum corneum* ceramide profile and skin barrier function in lesional and non-lesional skin of MF patients and in healthy volunteers, and to assess the effect of topical treatment with chlormethine gel on the ceramide profile.
Methods 21 early-stage MF patients and 10 healthy volunteers participated in the study. Ceramides were collected by tape stripping at baseline and after 16 weeks of treatment with chlormethine gel and analyzed using liquid chromatography-mass spectrometry. Barrier function was assessed by measuring transepidermal water loss.
Results The ceramide profile of lesional skin in MF was significantly different from non-lesional and healthy skin and correlated with the reduced barrier function. Specifically, lesional skin showed an altered ceramide subclass composition and a reduction in average ceramide chain length. These changes were partially normalized with chlormethine treatment, particularly in patients with a good treatment response.
Conclusion MF lesions exhibit a distinct and altered ceramide profile compared to non-lesional and healthy skin, which can partially be restored with topical chlormethine treatment.

9 – NOOR VAN HOUT

CONSTRUCTION OF A MINIMAL SKIN MICROBIOME AS A TOOL TO STUDY MICROBE-MICROBE INTERACTIONS

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Background The skin microbiome plays a key role in maintaining skin health, and its imbalance contributes to inflammatory skin diseases such as atopic dermatitis (AD), often marked by *Staphylococcus aureus* dominance.
Objective To investigate microbe-microbe interactions within a minimal skin microbiome by developing selective culture methods that allow quantification of individual bacterial strains from mixed communities after co-culture with skin models.
Methods Four skin-associated bacteria were selected, three commensal species (*Cutibacterium acnes*, *Staphylococcus epidermidis*, *Corynebacterium striatum*), and one pathogenic strain (*Staphylococcus aureus*). Mixed samples in 1:1:1:1 ratios were plated on selective agar plates under varying conditions to enable differentiation of colony-forming units per species. Tested parameters included pH modification, antibiotic overlays, incubation temperature, and colorimetric selection.
Results Acidification of LB agar to pH 4.6 selectively inhi-

bited *C. striatum* growth, facilitating separation from both *Staphylococcus* species. Overnight incubation at room temperature inhibits the growth of *S. epidermidis*, allowing to count the amount of *S. aureus*. Furthermore, an afabicin overlay effectively inhibited Staphylococci, allowing quantification of *C. acnes* and *C. striatum*. Because *C. acnes* only grows anaerobically, the amount of *C. striatum* can be determined under aerobic culturing conditions.
Conclusion By combining abiotic, antibiotic, and colorimetric selection strategies, we established a reproducible method to quantify individual alive bacterial populations within a defined minimal skin microbiome. These optimized separation techniques can support future studies on microbe–microbe interactions and the growth dynamics of potential therapeutic probiotic strains on human epidermal equivalents.

10 – FLORENCE VROMAN

THE DIFFERENTIAL EFFECT OF DUPILUMAB AND JAK INHIBITORS ON THE SKIN MICROBIOME IN PATIENTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS IN DAILY PRACTICE: DATA FROM THE BIODAY REGISTRY

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Background Atopic dermatitis (AD) is associated with reduced skin microbial diversity and increased *Staphylococcus aureus* (*S. aureus*) colonization. Dupilumab has shown to improve skin microbial diversity and lower *S. aureus* abundance in AD patients; however, less is known on the effect during Janus kinase 1-selective inhibitor (JAK1-i) treatment.
Objective To evaluate the effect of JAK1-i compared to dupilumab on the skin microbiome of AD patients aged 12 years and older.
Methods Skin swabs were collected from AD patients: for dupilumab (n=20) lesional/non-lesional at baseline (T0) and week 16 (T16); for JAK1-i (n=15) lesional/non-lesional at T0, week 4 (T4) and 28 (T28); and for healthy controls (n=27). Relative abundance and microbial diversity were analyzed using shotgun sequencing.
Results In both groups, Eczema Area Severity Index (EASI) scores significantly decreased over time, indicating good clinical response. For dupilumab, in lesional skin, a significant decrease of *S. aureus* was observed at T16 compared to T0 (Log Fold Change (LFC) of 7.6). However, in JAK1-i treated patients, a less apparent, non-significant decrease of *S. aureus* was observed at T28 compared to T0 in lesional skin. In addition, during dupilumab treatment, a shift in microbial profiles and increase in diversity was observed, which revealed a shift towards that of HCs. This was less evident in JAK1-i treated patients.
Conclusion Although both dupilumab and JAK1-i treatment resulted in a comparable clinical effect, the skin microbiome of AD patients treated with dupilumab shifted towards that of healthy skin, while this effect was not observed during JAK1-i treatment.

11 – RINDERT VENEMA

DEVELOPMENT OF A HUMAN ANTI-HUMAN-DESMOGLEIN-3 (HU-A-DSG3) MONOCLONAL ANTIBODY FOR TARGETED SYSTEMIC DELIVERY TO THE SKIN

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Background Despite advances in skin gene therapies for genodermatoses such as recessive dystrophic epidermolysis bullosa (RDEB), effective delivery continues to be a major hurdle. Previously, we developed antisense oligonucleotide mediated exon skipping for RDEB, however, optimization of delivery is essential for exon skipping to be a viable approach for systemic treatment of RDEB. Therefore, we use exon skipping for RDEB as use case for the development of a universal targeted systemic delivery platform for the skin, which could be beneficial for RDEB and translated to other skin related diseases.
Objective Develop a universal targeted systemic delivery platform for the skin, by capturing the genetic sequence of hu-a-dsg3 targeting B-cells of Pemphigus Vulgaris (PV) patients.
Methods To capture the genetic sequence of hu-a-dsg3 B-cells, we isolated peripheral blood mononuclear cells from PV patients and stained for B-cell markers and AF647-labelled recombinant DSG3. Next, cells were single cell sorted by FACS and stimulated for antibody production for two weeks. A DSG3 ELISA was performed for IgG producing colonies, where positives were selected for RNA isolation, templated switching oligo cDNA conversion and nested PCR to obtain the B cell receptor sequence. Next, we re-expressed this sequence in plasmids designed for antibody production and produced the monoclonal hu-a-dsg3 delivery platform in HEK293T cells. Lastly, the hu-a-dsg3 antibody was characterized by extensive *in vitro* diagnostic assays.
Results/Conclusion We have successfully isolated and expressed a monoclonal hu-a-dsg3 antibody which lays the foundation for the development of a universal delivery platform for gene therapies as antisense oligonucleotides.

12 – TARA URSELMANN

MULTI-MODAL INTEGRATIVE SINGLE CELL RNA-SEQUENCING BASED ATLAS OF CHRONIC INFLAMMATORY SKIN DISEASE

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Background Current treatment of chronic inflammatory skin disease patients is trial-and-error based. This one-size-fits-all strategy fails to consider stratification biomarkers and overlooks potential shared mechanisms across diseases and repurposing of established drugs. Growing research efforts directed to atopic dermatitis (AD), Psoriasis (PSO), and more recently Hidradenitis Suppurativa (HS) have yielded multiple publicly available single-cell RNA-sequencing (scRNAseq) datasets of patient skin biopsies. Inclusion of both lesional and non-lesional samples, and treated patients enables high resolution investigations into cell-specific transcriptome-based mechanisms.
Objective To identify and integrate scRNAseq datasets of AD, PSO, and HS to build a computational tool able to visualize gene expression, including pathway activity scores and user-provided module scores to deepen atlas capabilities.
Methods Datasets were extracted from databases and processed through the Seurat pipeline. The data was integrated with Harmony and visualized by UMAP. Pathway activity was calculated with the PROGENy package.
Results We successfully constructed a single cell atlas through data curation and subsequent integration, resulting cells to cluster by cell type, enabling comparison between diseases. Pathway activity analysis was validated by JAK-STAT upregulation in AD, and revealing it as a shared mechanism across all three diseases. In contrast, TNFα pathway activity differentiated the diseases, showing elevated activity in keratinocytes from HS patients, while it was primarily upregulated in fibroblasts from PSO patients. Future research will focus on experimental validation and enrollment of the tool for public access.
Conclusion Our successful data integration enables identification of cell-specific mechanisms between chronic inflammatory skin diseases to improve personalized treatment.

13 – WEIXIN ZHOU

TRANSCRIPTOME ANALYSIS REVEALS A DISTINCT MOLECULAR PROFILE OF HYPERKERATOTIC HAND ECZEMA

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Background Hyperkeratotic hand eczema (HHE) is a clinical subtype of hand eczema, but emerging evidence suggests distinct pathophysiology.
Objective To profile the transcriptomes of HHE and compare these profiles with psoriasis and atopic dermatitis.
Methods Biopsies were obtained from lesional and non-lesional palmar skin of 11 adult patients with moderate-to-severe HHE and from the central palmar regions of 11 HC. Differentially expressed genes (DEGs) were identified using RNA sequencing (|fold change| > 2.0, false discovery rate < 0.01), with pathway enrichment analysis via KEGG/REACTOME databases. Gene set variation analysis (GSVA) facilitated comparison between lesional skin, non-lesional skin, and HC, as well as comparative analysis with GSE121212 dataset of psoriasis and atopic dermatitis transcriptomic data, obtained from body sites other than the hands.
Results RNA-seq revealed 2329 DEGs between lesional skin and HC and 318 between non-lesional skin and HC. Upregulated genes in lesional skin included T-cell activation markers (TNFRSF4, IL2RA), pro-inflammatory mediators (IL36G/20/23A), and chemokines (CXCL9/10, CCL18). Downregulated genes included lipid metabolism regulators (PLIN1, CIDEC) and barrier components (CLDN7/8/10). GSVA revealed increased Th1/Th2/Th17/Th22 activation, enhanced IL-12/23 and IL-36 signalling, increased tissue resident memory T cell (TRM) signatures and impaired lipid barrier and tight junction pathways in lesional skin. HHE exhibited broader T-helper activation than the Th17/IL-36-dominant profile of psoriasis and the Th2/JAK-STAT-driven signature of atopic dermatitis, with more pronounced TRM enrichment and barrier dysfunction.
Conclusion HHE is a distinctive entity with transcriptomic positioning between psoriasis and atopic dermatitis, implying a potentially unique pathophysiology.

14 – ASHLEIGH JIMENEZ LEMUS

HIGH PREVALENCE OF CUTANEOUS POSTZYGOTIC MOSAICISM OF PATCHED 1 VARIANTS IN PATIENTS DEVELOPING MULTIPLE BASAL CELL CARCINOMAS

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Background Basal cell nevus syndrome (BCNS) is a rare genetic disorder, characterized by multiple basal cell carcinomas (BCCs) and associated syndromic features. BCNS results from heterozygous pathogenic variants in the Patched 1 (PTCH1) tumor suppressor gene. Causal germline PTCH1 variants are well established in BCNS, however the prevalence of postzygotic mosaicism for PTCH1 variants in cutaneous BCC cases remains unclear.
Objective We aimed to investigate PTCH1 mosaicism prevalence in a cohort of patients with multiple BCCs and other BCNS features, lacking germline PTCH1 mutation in blood.
Methods Multiple different BCCs from 42 patients suspected having BCNS, lacking a germline causal PTCH1 variant in blood, were genotyped for PTCH1 using targeted next-generation sequencing. This cohort study was complemented by a literature review on PubMed, LOVD and EMBASE, to conceptualize the prevalence of de novo PTCH1 variants in BCNS.
Results Literature review demonstrated that the prevalence of de novo mutations in BCNS patients account for 35.8%. This suggests that mosaicism may be more prevalent in the general population than earlier acknowledged. Accordingly, in our cohort of patients with suspected BCNS, we found 33% of patients with postzygotic mosaicism in PTCH1, sharing a variant in the patient's BCCs. Remarkably, these patients frequently exhibit only multiple BCCs, with no other manifestations of BCNS.

Conclusion We demonstrate by using this analytic strategy, that many of the so called high frequency BCC patients are ultimately diagnosed as postzygotic PTCH1 mosaic cases. PTCH1 mosaicism may represent a significant proportion of patients with unexplained occurrence of multiple BCCs.

15 – ROSALIE BAARDMAN

TOWARDS AN OPTIMAL DIAGNOSTIC STRATEGY FOR EPIDERMOLYSIS BULLOSA (EB): THE DIAGNOSTIC AND PROGNOSTIC VALUE OF EB DIAGNOSTIC MODALITIES

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Background Epidermolysis bullosa (EB) comprises a heterogeneous group of rare disorders featuring mucocutaneous fragility. Currently, the diagnostic modalities for EB encompass: clinical assessment, immunofluorescence microscopy (IFM), transmission electron microscopy (TEM) and genome diagnostics (GD).
Objective To evaluate the diagnostic performance of clinical assessment, IFM, TEM, and GD in determining (1) main EB-type and (2) EB-subtype, and (3) to assess the added value of microscopy to GD.
Methods Patients with genetically confirmed EB-diagnoses who had IFM and TEM performed between 1988-2023 were retrospectively included. The proportion of cases in which the outcomes of the EB-diagnostic modalities matched for (1) main EB-type and (2) EB-subtype was calculated across the entire cohort, subdivided by EB-(sub)type and age. The reference standard for main EB-type was the identified pathogenic gene aligning with initial clinical phenotype and for EB-subtype the final EB-diagnosis. To evaluate the added value of IFM and TEM over GD, we assessed cases where IFM or TEM matched the final EB-diagnosis in cases where GD did not.
Results We included 202 patients. Initial clinical assessment, IFM and TEM matched main EB-type in 80.7%, 81.7% and 89.1%. Regarding EB-subtype: initial clinical assessment, IFM, TEM and GD matched in 41.1%, 29.7%, 12.9% and 55.4%. The added value of microscopy to GD in EB-subtyping was 6%. Additionally, IFM performed best in neonates and junctional EB.
Conclusion The EB-diagnostic modalities showed higher diagnostic than prognostic value, with GD excelling. Notably, IFM exhibited the highest prognostic value in neonates, highlighting its continued critical role in daily clinical practice.

16 – FAUVE VAN VEEN

REPRODUCTIVE DILEMMAS IN GENODERMATOSES: INTERNATIONAL PERSPECTIVES OF COUPLES/PATIENTS, CAREGIVERS, DERMATOLOGISTS AND CLINICAL GENETICISTS

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Background Inherited skin disorders (genodermatoses) impact patients' quality of life. Given the chronicity of genodermatoses and risk of transmission, couples/patients considering parenthood may face reproductive dilemmas. However, very little is known about this topic.
Objective To understand the reproductive decision-making (RDM) process: 1) Explore the impact of genodermatoses on couples/patients' RDM, their knowledge of and experience with reproductive options and counseling. 2) Examine clinical practice of professional support in RDM, from dermatologists and clinical geneticists' perspectives. 3) Assess the caregiver burden for those caring for patients with genodermatoses.
Methods Two qualitative studies were conducted: 1) with affected couples/patients, and 2) with dermatologists and clinical geneticists working in the Netherlands, Belgium, Australia and Japan. A scoping review was performed to investigate the perceived caregiver burden.
Results Interviews with couples/patients (n=30) revealed that most participants preferred to prevent transmission and considered reproductive options like pre-implantation genetic testing (PGT). RDM was influenced by negative experiences and fear about severe manifestations in offspring. Routine reproductive counseling was inadequate. Preliminary

findings from interviews with dermatologists and clinical geneticists (n=20) showed limited awareness among dermatologists regarding when to discuss reproductive options (e.g., PGT), alongside uncertainty about their counseling role for different genodermatoses. Clinical geneticists, while skilled in counseling, often lacked detailed knowledge of genodermatoses. The scoping review (54 included studies) showed variable attention from researchers per group of genodermatoses and a multifaceted impact on caregivers, influencing their quality of life and RDM.
Conclusion Genodermatoses substantially affect RDM, underscoring the need for routine reproductive counseling, improved education and interdisciplinary guidelines.

17 – DAPHNE PANOCHA

A HUMAN IMMUNOCOMPETENT LN-SCAFFOLD MODEL TO STUDY HUMAN IMMUNE RESPONSES

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Background Fibroblastic reticular cells (FRCs) arrange the dense lymph node (LN) architecture and are required for LN functioning. However, to date, current human *in vitro* LN models do not accurately mimic the aspects of human LN physiology while simultaneously allowing the long-term culture of FRCs in an *in vitro* model, which is needed to study the human immune system.
Objective In this study we aim to develop a human LN model using pre-printed scaffolds, comprising of FRCs and autologous immune cells from human LNs, for the long-term culture of FRCs and immune cells.
Methods Human FRCs and immune cells were isolated from LN biopsies. Pre-printed scaffolds were coated with collagen type 1 and first seeded with FRCs, followed by autologous immune cells. After 21 days of culture, flow cytometry, confocal imaging and cytokine/chemokine analysis were performed.
Results The LN-scaffold model resulted in viable cultures for up to 21 days and enabled close contact between FRCs and immune cells. FRC maintained their expression of important cell surface markers and the LN-scaffold supported the culture of several immune cell subsets. Furthermore, the microenvironment formed in the LN-scaffold model showed physiological similarities to the *in vivo* LN niche, consisting of extracellular matrix and the relevant cytokines and chemokines needed for immune homeostasis.
Conclusion This study demonstrates the relevance of LN-scaffolds for properly mimicking LN physiology. These findings support the suitability of the LN-scaffold model for multi-organ-on-chip set-ups, such as a skin-draining LN model to study human immune responses downstream from dermal pathology.

18 – ALESHA LOUIS

DISSIMILAR ROLES FOR PAPILLARY AND RETICULAR FIBROBLASTS IN SKIN PIGMENTATION: INSIGHTS FROM 3D IN VITRO HUMAN FIBROBLAST DERIVED MATRIX MODELS

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Background Human dermis is separated into the papillary (Pfs) and the reticular (Rfs) layer and with age a relative increase in the reticular layer has been observed. Skin aging is associated with the development of pigmented lesions, and since pigmentation is regulated by multiple pathways, distinct roles for Pfs and Rfs are hypothesized. Interestingly, transcriptomic studies suggest that the skin microbiome may influence pigmentation. Melanocytes can affect the composition of the skin microbiome, while the microbiome itself plays a role in melanocyte survival. Both the composition of the skin microbiome and the structure of the dermal layers changes with age, which may impact pigmentation. Therefore, in this study, we investigated the role of Pfs, Rfs and the skin microbiome on skin pigmentation.
Objective To explore the combined impact of Pfs, Rfs and microbiome shifts on skin pigmentation.
Methods Human skin equivalents (HSE) generated with Pfs or Rfs, and inoculated with *Staphylococcus (S.) epidermidis* were analyzed for epidermal morphogenesis and melanogenesis-related pathways.
Results Pf-HSE demonstrated an enhanced epidermal structure compared to Rf-HSEs. Rf-HSE have increased numbers of melanocytes in the basal layer, increased melanin and distinct expression of melanogenesis-related genes compared to Pf-HSE. *S. epidermidis* seem to increase melanocyte number although its exact role in melanocyte survival and skin pigmentation needs to be elucidated.
Conclusion We reveal dissimilar roles for Pfs and Rfs and the skin microbiome in skin pigmentation and melanogenesis-related pathways. Further investigation is warranted to validate the role of Pfs, Rfs and the skin microbiome in skin pigmentation.

19 – JAIMY KLIJNHOUT

A COMPARATIVE ANALYSIS OF N/TERT-DERIVED EPIDERMAL EQUIVALENTS

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Background N/TERT immortalized keratinocyte cell lines share key epidermal characteristics with primary keratinocytes in human epidermal equivalents (HEEs). Over the past 25 years, their widespread use in experimental dermatology has led to increasing variability in cell culture protocols, complicating cross-study comparisons.
Objective To compare N/TERT HEEs generated using EpiLife, KSFM, CELLnTEC or in-house developed media to *in vivo* epidermis based on morphology and epidermal gene- and protein expression.
Methods Formalin-fixed paraffin-embedded HEEs from two collaborating laboratories were assessed on morphology, and proliferation and differentiation protein markers, including Ki67, keratins 2, 10, 15 and 16, filaggrin, involucrin, transglutaminase-1 (TGM-1) and cathepsin V (CTSV). RNA sequencing was performed on EpiLife and CELLnTEC cultures to identify differentially expressed genes.
Results All culture protocols generate a multilayer stratified epidermis. EpiLife-generated HEEs have 5-6 epidermal layers and a cobblestone-like basal layer. Other models contain 6-8 cell layers and a less pronounced basal morphology. Ki67 staining confirms differences in proliferation rates between media and differentiation marker expression varies between models. A lower proliferation rate correlated with more *in vivo*-like differentiation patterns and higher expression of terminal differentiation proteins TGM-1 and CTSV. Transcriptomic analyses will aid in discovery of biological processes linked to observed phenotypes and correlations to culture medium composition.
Conclusion EpiLife-generated HEEs show the closest morphological resemblance to *in vivo* epidermis. Additional analyses on gene- and protein expression and barrier function are necessary and ongoing to draw final conclusions on best practices. Hereby we will steer our experimental dermatology field towards improved and reproducible epidermal models.

20 – JOLIENE WICHERS SCHREUR

DISSECTING THE IMPACT OF CTCL T-CELL LINES ON EPIDERMAL STRUCTURE AND FUNCTION

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Background Cutaneous T-cell lymphomas (CTCL) are a group of rare malignancies characterized by the presence of malignant T-cells in chronically inflamed skin lesions. In early stages, CTCL lesions often mimic benign inflammatory dermatoses. As the disease progresses, skin lesions evolve in tumors and/or generalized erythroderma. The pathogenesis and pathophysiology of CTCL is not fully understood. In particular, little is known about how the altered cytokine milieu in CTCL affects the epidermal compartment. This knowledge gap hampers the development of effective, targeted therapies and limits our ability to stratify patients based on disease behavior.
Objective This study aims to unravel the effect of cytokines secreted by malignant CTCL T-cell lines on epidermal morphogenesis, architecture, and barrier function, with the goal of clarifying their role in disease progression and skin pathology.
Methods 2D cell cultures and 3D human skin equivalents (HSEs) were generated and exposed to varying concentrations of conditioned media from malignant CTCL T-cell lines (HH, MyLa, and SeAx) during the final 72 hours before harvesting. Epidermal morphogenesis, structure and function were assessed based on morphology and epidermal markers.
Results Morphological analysis demonstrated that secreted cytokines from CTCL T-cell lines impaired keratinocyte differentiation. The expression of barrier markers was reduced indicating that cytokine exposure altered epidermal stratification and barrier formation.
Conclusion Cytokines from malignant CTCL T-cell lines impair epidermal morphogenesis, structure and function in both 2D keratinocytes cultures and 3D HSEs. Ongoing in-depth analysis aims to further validate the functional consequences of these cytokines and their role in CTCL-associated epidermal pathology.

21 – RENS PETERS

COMBINING EXPERIMENTAL AND AI-DRIVEN APPROACHES FOR DEVELOPING IMMUNOCOMPETENT 3D SKIN MODELS

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Background Common inflammatory skin disease, like atopic dermatitis (AD) are characterized by epidermal barrier disruption and T-helper cell-driven inflammation. Integrating relevant immune subsets into physiologically relevant 3D skin models enables disease-specific immune–epithelial cellular crosstalk, improving disease modeling and therapeutic testing.
Objective We aimed to establish an immunocompetent *in vitro* AD skin model incorporating Th2-polarized T-cells within a collagen-based dermal compartment.
Methods Systematic development of AI prompts, trained and validated on relevant datasets, enabled efficient data extraction by ChatGPT to map existing 2D and 3D immunocompetent skin models. Highlighted common practices and limitations in immune cell integration strategies were utilized to improve cell culture protocols for 2D co-cultures of keratinocytes with fibroblasts or T-cells, and 3D skin models with activated T-cells.
Results Literature revealed inconsistent approaches to Th2-

cell polarization and immune-cell integration, which guided the optimization of our model design. Protocols were optimized to successfully isolate keratinocytes, fibroblasts, and skin-resident T-cells from one single human skin biopsy, enabling donor-matched model construction. T-cells stimulated keratinocytes to secrete CXCL10, CCL2, and CCL20 chemokines in a dose-dependent manner. Activated T-cells induced epidermal differentiation disruption and upregulation of inflammatory markers, reflecting early AD-like pathology. Optimized polarization protocols yielded Th2 cells (IL-4 and GATA3 expression) in >50% of naïve $CD4^+$ T cells, to incorporate in co-culture models.
Conclusion By combining AI-guided literature searches and data extraction, with experimental validation, we established the foundation for immunocompetent 3D skin models incorporating Th2-polarized T cells—an essential step toward physiologically relevant *in vitro* models of atopic dermatitis.

22 – MARIE CHEVALIER FLORQUIN

MAPPING THE SPATIAL IMMUNE LANDSCAPE IN SEZARY SYNDROME: INSIGHTS INTO MODERATE AND PROGRESSIVE PROGNOSES

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Background Sezary syndrome is a rare (<5% of cutaneous T-cell lymphomas) and aggressive malignancy, characterised by erythroderma, lymphadenopathy, and clonally related neoplastic T cells ('Sezary cells') in skin, lymph nodes, and blood. Median survival is 32 months, with 5-year survival of 10–30% [1]. While the extent of peripheral blood involvement may affect prognosis [2], the prognostic significance of the skin tumour microenvironment (TME) remains unclear.
Objective To characterise the spatial TME in Sezary syndrome across patient samples with differing survival to identify immune cell dynamics and potential prognostic markers.
Methods Spatial transcriptomics was performed on 18 FFPE baseline biopsies from patients with long-term (≥5 years, n=4), intermediate-term (2–5 years, n=8), and short-term (≤2 years, n=6) survival, and 4 follow-up samples from patients with short-term survival showing progression under treatment (mogamulizumab, n=3; interferon, n=1). Analyses used the Xenium platform (10x Genomics) with an immune-oncology panel (n=380) and a custom panel (n=95). Cell segmentation was performed with the Xenium Cell Segmentation Kit, and cell type annotation combined reference-based typing [3] with clustering. Neighbourhood analyses will be performed using an in-house computational pipeline.
Results Preliminary spatial profiling of 18 samples suggests variation in immune and stromal cell organisation across prognostic groups, including differences in B-cell and cytotoxic cell levels. These findings are being explored in ongoing analyses to clarify biological and prognostic relevance.
Conclusion Spatial mapping of Sezary syndrome reveals prognostic group–specific variation in the skin TME. Further analyses will determine how these spatial immune patterns relate to disease progression and outcomes.

23 – ANDRYA REDER HOLLATZ

A PREDICTION MODEL FOR A FIRST METACHRONOUS CUTANEOUS SQUAMOUS CELL CARCINOMA: A 10-YEAR NATIONWIDE COHORT STUDY

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Background Following a first cutaneous squamous cell carcinoma (CSCC), one-third of patients develop new primaries, yet individualized absolute-risk estimates to guide follow-up are limited.
Objective To develop and internally validate a competing-risk model predicting the first metachronous CSCC after an index CSCC.
Methods A retrospective nationwide cohort study including patients with a first histologically confirmed CSCC in 2007–2008 (Netherlands Cancer Registry) with up to 10-years of follow-up. We developed a Fine–Gray competing-risk model for the first metachronous CSCC using prespecified predictors (age, sex, hematologic malignancy, basal cell carcinoma (BCC) and actinic keratosis (AK) history, synchronous CSCC, tumor location and differentiation). We evaluated model performance via time-dependent C-index and calibration measurements after 10-fold cross-validation.
Results Among 11,737 patients (median age 76 years; 57% male), 3,288 (28%) developed a metachronous CSCC. Strong predictors included AK history, ≥5 prior BCCs, and history of chronic lymphocytic leukaemia/small lymphocytic leukaemia; male sex, synchronous CSCC, sun-exposed sites, and poorer differentiation were also associated with higher risk. Cross-validated 5-year C-index was 0.64 with good calibration.
Conclusion A competing-risk model using routinely available clinical features provides well-calibrated absolute-risk estimates for metachronous CSCC, supporting future risk-based surveillance research despite modest discrimination.

24 – INGER KREUGER

SPATIAL GENE EXPRESSION AND MICROENVIRONMENTAL CHANGES IN THE TRANSITION OF NEVUS TO MELANOMA

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Background Melanoma is an aggressive skin cancer, which can arise from benign nevi. Enhancing our understanding of melanoma development from nevi could improve early diagnosis and treatment. However, studies of early melanoma stages are limited, and the existing studies were mainly performed using bulk RNA sequencing, involved only limited gene subsets, or lacked spatial context.
Objective Therefore, we have mapped the transition of nevi to melanoma using spatial transcriptomics.
Methods We analyzed nevus-associated melanoma FFPE samples from 18 patients using the 10X Genomics Visium Spatial Gene expression technology. Data analysis was conducted using Spaceranger, Semla, STdeconvolve and various R packages. Additionally, imaging mass cytometry was performed.
Results We identified the main transcriptomic signatures in the skin, as well as nevus an melanoma signatures and their spatial location. Differential gene expression analysis identified potential biomarkers and key pathways in melanoma. The pathways could be broadly classified into three major categories: promoting proliferation under metabolic stress, alterations in differentiation state, and modifications linked to microenvironmental remodelling. Additionally, two melanoma signatures within the same patient with their own spatial location were detected. Microenvironmental analysis further showed shifts in immune cells, with only M2-like macrophages in the nevus, but abundant immune cells around melanoma regions. Simultaneously, melanomas exhibited features associated with an immunosuppressive microenvironment.
Conclusion Spatial analysis revealed gene expression alterations and microenvironmental changes during the transition of nevus to melanoma. This study advances our understanding of melanoma development, thereby providing a framework for the identification of novel biomarkers and treatment targets in melanoma.

25 – ALEX ROOKER

PTCHFLOX/FLOXERT2+/– MOUSE MODEL DRIVES HAIR FOLLICLE NEOPLASMS RATHER THAN BASAL CELL CARCINOMA

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Background Basal-cell carcinoma (BCC) is the most common skin cancer. Primary BCC-risk factors are UV-exposure and aging. Although BCC rarely metastasizes, its high and increasing prevalence creates an enormous healthcare burden. Immunotherapies such as checkpoint inhibitors have recently been introduced for locally advanced BCC but the immune system's natural role in BCC control remains poorly understood.
Objective Here we aim to investigate *in vivo* if BCC can be treated using a vitiligo bystander immune reaction against melanocytes present in BCC.
Methods Using an previously reported BCC model, Ptchflox/floxERT2+/– mice were injected with tamoxifen inducing BCC formation on the ear. During BCC development mice were either treated with monobenzone/imiquimod/CpG therapy (MIC) or vaccinated with TRP-2 peptide to induce vitiligo-like immunity.
Results Sixty days after induction, mice developed swelling and scab-like lesions on the ears, indicative of BCC lesions. Additionally, blood analysis showed that the MIC treated mice had T-cell activation and the vaccinated mice had a TRP2 specific T-cell response. However, histological examination by trained (mouse) pathologists, showed that ear-lesions resembled hair follicle neoplasms rather than fully developed BCC. Additional immunohistochemical staining using discriminative markers CD10, SOX9, Melan-A and EpCam, indeed confirmed these findings.
Conclusion Although we showed that vitiligo-inducing therapies generated a melanocyte specific T-cells response in mice, resulting in fur-depigmentation, our histopathological analysis revealed that the Ptchflox/floxERT2+/– BCC model produces hair follicle neoplasms rather than BCC. These findings emphasize the need for a well-characterized mouse model representative of human BCC to advance research into pathogenesis and immunotherapy of BCC.

26 – VEERLE MERKUS

STAGE-SPECIFIC CHANGES IN THE SPATIAL IMMUNE LANDSCAPE OF MYCOSIS FUNGOIDES

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Background Mycosis Fungoides (MF) is characterized by the proliferation of malignant CD4+ T cells. Disease progress occurs from early stage plaques (IA-IB) to late stage tumors

(IIb) in approximately one-third of cases. While recent research has explored the role of the tumor microenvironment (TME) in MF progression, spatial interactions between cancer cells and surrounding immune cells remain poorly understood.

Objective We aimed to profile the spatial landscape of the MF TME across disease stages, providing insight into immune cell dynamics and potential therapeutic targets.

Methods We performed a high-dimensional analysis of cell composition and interactions across MF stages using a custom Imaging Mass Cytometry (IMC) panel to examine the spatial complexity of the TME. 27 skin biopsies from 20 patients with confirmed classical CD4+ MF (stages IA- IIb) were included.

Results The IMC panel enabled visualization and identification of immune cell subsets, and revealed the cellular composition of MF tumors and plaques. Our findings revealed stage-specific changes, with early-stage plaques enriched in percentage of cytotoxic CD8+ T cells, whereas late-stage tumors exhibited increased B cell infiltration. We identified a shift from CD8+ T cell-cancer cell and monocyte-cancer cell interactions in plaques to B cell-cancer cell interactions in tumors.

Conclusion A stage-dependent shift in cellular interactions from an effective anti-tumor immune responses to features consistent with immune evasion mechanisms is observed during MF progression. These insights underscore the importance of spatial context in understanding MF progression and highlight therapeutic targets that could lead to stage-specific (immuno)therapies, ultimately improving patient outcomes.

27 – JULIETTE SIMONS

PERFORMANCE OF CICLOSPORIN IN OMALIZUMAB-NAÏVE AND OMALIZUMAB-REFRACTORY CHRONIC URTICARIA IN DAILY PRACTICE

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Background Ciclosporin is currently a second-line treatment for chronic urticaria (CU) patients. Effectiveness is mainly investigated in omalizumab-naïve populations.

Objective We aim to investigate the effectiveness and safety of ciclosporin in omalizumab-refractory CU-patients and for comparison in omalizumab-naïve patients, including factors associated with effectiveness.

Methods All CU-patients prescribed ciclosporin in two Dutch tertiary centers were retrospectively included. Response to ciclosporin (based on UCT or physician estimation), treatment duration, reasons for discontinuation, drug survival and potential predictors (Log/Cox regression) were assessed.

Results 166 CU-patients treated with ciclosporin were identified (68.7% female, median age 34 years). Complete/good response to ciclosporin was observed in 48% (n=75)(57.4% omalizumab-refractory patients, 40.9% omalizumab-naïve (p=0.04)). Ciclosporin-omalizumab combination treatment was used in 41% (n=68; median 3.8 months), mostly omalizumab-refractory patients (n=42). In 35% complete/good response (n=27/75) was attributed to combination treatment. Ciclosporin treatment was discontinued in 133 patients (80%). Reasons for discontinuation differed between omalizumab-naïve and omalizumab-refractory patients (p=0.15) respectively: remission 24% vs. 43%, side-effects 27% vs. 14%, ineffectiveness 19% vs. 11%, combination side-effects/ineffectiveness 24% vs. 27%. Ciclosporin drug survival rates due to remission at 0.5, 1 and 2 years differed significantly between omalizumab-naïve and omalizumab-refractory patients: 94%, 83%, 72% versus 91%, 67%, 35%)(p=0.004). Angioedema was associated with complete/good response to ciclosporin (OR 3.1 (1.6-6.2), p=0.001) and a lower risk of discontinuation due to ineffectiveness (HR 0.5 (0.3-0.9), p=0.02).

Conclusion Omalizumab-refractory patients show more often complete/good response and a more favorable drug survival, compared to omalizumab-naïve patients. Side-effects and ineffectiveness are common reasons for discontinuation, especially in omalizumab-naïve patients.

28 – CHARLOTTE VAN RIEL

DOSE REDUCTION OF IL-17 AND IL-23 INHIBITORS IN PATIENTS WITH PLAQUE PSORIASIS IS NON-INFERIOR TO USUAL CARE: AN INTERNATIONAL PRAGMATIC RANDOMIZED CONTROLLED TRIAL – THE BENEBIO STUDY

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Background Dose reduction of biologics for psoriasis may lower costs and prevent overtreatment. Knowledge on dose reduction of the newest biologics, interleukin (IL)17 and IL23 inhibitors (i), is lacking.

Objective This pragmatic, non-inferiority randomized clinical trial evaluates whether dose reduction (DR) by stepwise interval prolongation of IL17i and IL23i in patients with psoriasis with stable low disease activity is non-inferior to usual care (UC).

Methods A total of 244 patients using IL17i/IL23i with stable low disease activity and good quality of life at inclusion, were randomized 2:1 to DR (stepwise interval prolongation to 67% and 50% of standard dose) or UC. Primary outcome: difference in cumulative incidence of persistent flares (PASI>5 for ≥3 months) after 18 months with a 15% non-inferiority margin. Secondary outcomes: proportion of patients with successful DR, course of PASI/DLQI, and safety.

Results At baseline: mean(±SD) age 51(±15) years, 67% male, 46% used IL17i, 54% used IL23i, 47% was biologic naive, and median[IQR] PASI and DLQI were 0.0 ([1.1] and [1.0], respectively). After 18 months, the difference in cumulative incidence of persistent flares for DR was non-inferior to UC (0.62% (95%CI [-5.84%; 4.64%]). Also, 74.5% of patients had a successful DR.

Mean PASI and DLQI scores were very low and did not significantly differ between DR and UC. No safety signals related to DR were detected.
Conclusion Dose reduction of IL17i and IL23i in psoriasis patients with low disease activity was non-inferior to UC and safe. At 18 months, successful DR was reached in ¾ of patients.

29 – SARA VAN DER KAMP

PERFORMANCE OF OMALIZUMAB IN PATIENTS WITH MAST CELL-MEDIATED ANGIOEDEMA

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Background Mast cell–mediated angioedema (AE-MC) is managed according to urticaria guidelines. Evidence on the efficacy and safety of omalizumab has mainly been derived from RCTs including patients with mainly wheals (with/without AE-MC) or small case series.
Objective To investigate long-term real-world performance of omalizumab in patients with isolated or predominantly AE-MC.
Methods In this retrospective multicenter cohort study, 14 international urticaria expertise centers included all AE-MC patients treated with omalizumab (data lock 2022). Treatment response was assessed using UCT and physician assessment. Drug survival by reason for discontinuation (Kaplan–Meier analysis) and predictors of treatment discontinuation (Cox regression) were analysed.
Results Of 148 patients with AE-MC (mean age 45; 74% female) who started omalizumab, 67 (45%) had isolated AE and 81 (55%) AE with subordinary wheals. The majority of all patients (77%, n=90/117) had good/complete response to omalizumab, without significant differences between subgroups. Overall, 60 (41%) patients discontinued, primarily due to well-controlled disease (63%, n=38); less frequent due to ineffectiveness (18%, n=11) or adverse effects (5%, n=3). Drug survival due to well-controlled disease was 82%, 67%, and 58% at 1, 2, and 5 years, respectively, independent of the presence of subordinary wheals. Longer disease duration prior to omalizumab (>2 years) predicted delayed discontinuation (HR 0.32), while fast response predicted earlier discontinuation (HR 2.71) due to well-controlled disease. No predictors for discontinuation due to ineffectiveness were found.
Conclusion Omalizumab is highly effective and safe in mast cell–mediated angioedema, independent from presence of wheals, supporting the management of AE-MC as part of CSU.

30 – IMKE VAN GINKEL

DEVELOPMENT OF A FLUORESCENCE MOLECULAR IMAGING METHOD FOR USTEKINUMAB IN PSORIASIS

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Background Fluorescence molecular imaging of the skin is a novel technique in dermatology, while its value has already been demonstrated in oncology and in gastroenterology. Promising results in molecular imaging of biologics for inflammatory bowel disease suggest similar potential in dermatological conditions.
Objective To develop a robust and reproducible imaging protocol enabling targeted imaging of biologics in psoriasis.

Methods Ustekinumab was conjugated with IRDye800CW under GMP conditions to ensure stability and suitability for clinical use. A custom-built in-house fluorescence camera was developed, and to enable quantitative analysis of the fluorescence signal, a complementary spectroscopy system was constructed. Additionally, a standardized protocol was established for ex vivo analysis of skin biopsies using fluorescence microscopy, allowing detailed visualization of tracer distribution in lesional and non-lesional skin. Subsequently, a clinical trial was initiated to evaluate the feasibility and performance of the complete imaging workflow in patients with psoriasis.
Results Eight imaging procedures have been successfully completed, with no adverse events reported. Preliminary analysis of fluorescence imaging data revealed strong light reflectance from the device on the skin, complicating image interpretation. However, spectroscopy measurements showed a clear increase in fluorescence intensity in lesional skin compared to non-lesional skin. Furthermore, tracer signal detection was successful using fluorescence microscopy.
Conclusion These preliminary data demonstrate the feasibility of detecting ustekinumab-800CW in patients with psoriasis with the developed method. The results highlight the potential of fluorescence molecular imaging as tool for visualizing drug distribution in dermatological conditions with potential implications for guiding personalized therapeutic strategies.

31 – YARA VALKENBURG

DYNAMIC VS. CONVENTIONAL OPTICAL COHERENCE TOMOGRAPHY FOR DIAGNOSING BASAL CELL CARCINOMA: A DIAGNOSTIC COHORT STUDY

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Background Optical coherence tomography (OCT) provides a non-invasive diagnostic alternative to biopsy for diagnosing basal cell carcinoma (BCC). Dynamic OCT (D-OCT), integrated into OCT-devices, visualizes vascular shapes and patterns using speckle-variance.
Objective This diagnostic cohort study evaluated whether D-OCT improves BCC detection and subtyping accuracy compared with OCT alone and which vascular shapes and patterns predict BCC presence and its subtype.
Methods Lesions clinically suspicious for BCC requiring biopsy were scanned using (D-)OCT. Scans were assessed in a paired order alongside clinical photographs; first the conventional scan, subsequently with visualization of vasculature at three standardized depths (150µm, 300µm, 500µm). Diagnostic confidence was assigned on a five-point confidence-scale, the predicted subtype was noted as well as the predominant vascular shape and pattern. Histopathology served as reference test.
Results A total of 321 patients with 424 lesions were included (BCC prevalence of 60.8%). D-OCT assessment resulted in a higher sensitivity for BCC detection compared to OCT (84.9% vs. 72.9%, respectively, p=<0.001), at comparable specificity (94.0% vs. 95.8%, respectively p=0.453). Diagnostic parameters for BCC subtyping were comparable between OCT and D-OCT assessment. Vascular shapes and patterns with either positive or negative associations for BCC detection and subtyping were identified.
Conclusion Using the dynamic functionality for blood vessel examination on OCT improves the sensitivity for BCC detection without compromising specificity. Although both positive and negative associations have been found between vascular shapes and patterns and the presence of BCC and its subtypes, D-OCT does not improve subtype classification accuracy compared to conventional OCT.